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The Relation Between Laparoscopic Sleeve Gastrectomy and Ghrelin

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ABSTRACT

Recently, obesity has become an important worldwide health problem. One of the obesity treatment alternatives is bariatric surgery methods and their efficiency is increasing from day to day. In laparoscopic Sleeve gastrectomy being a bariatric surgery method, as a result of stomach fundus excretion, levels of some hormones change. Therefore, weight losses seen after the treatment are related to these changes. Basically, it is claimed that, after laparoscopic Sleeve gastrectomy, levels of ghrelin hormones secreted by stomach fundus, being effective for appetite and getting foods change. Although there are many studies examining varieties of ghrelin levels after laparoscopic sleeve gastrectomy, there is no final judgment concerning the subject yet. In this review, in the light of literature knowledge, giving information regarding effects of laparoscopic sleeve gastrectomy on ghrelin levels is aimed.

Keywords: Bariatric surgery, Ghrelin, Sleeve gastrectomy

INTRODUCTION

Obesity is one of the most significant health problems seen on all age groups worldwide. Especially morbid obesity (Body Mass Index (BMI) ≥ 40 kg/m^2) is notified as an important risk factor for various diseases like type 2 diabetes, pulmonary dysfunction, cardiovascular diseases, and hypertension [1,2].

In that case many treatment approaches are applied in controlling obesity. Consuming adequate and balanced foods, life style alterations focusing on regular physical activities, medications are some of them. In addition, since the end of the years 1990 it has been started to emphasize that surgical treatments (bariatric/metabolic operations) are the most effective obesity treatments [1,2].

In this review, in the light of literature knowledge, especially giving information about the method of laparoscopic Sleeve gastrectomy being a bariatric surgery and results of this method on ghrelin levels is aimed.

What is Bariatric Surgery?

Bariatric surgeries are every kind of surgical applications, accepted as effective treatment methods which provide people with decreasing excessive body weight, for morbid obesity [2,3].

In consensus decisions in 1991, American National Health Institutes determined the necessary conditions for bariatric surgery. According to these decisions bariatric surgery indications [4]:

1. BMI >40 kg/m^2 or BMI > 35 kg/m^2 with accompanying disease (type 2 diabetes, hypertension, sleep apnoea, hyperlipidaemia).

2. The operation risk is acceptable.

3. Other treatments except for surgery are unsuccessful.

4. The patients should be well motivated and knows the operation and its shekels.

5. There should be no medical problem as a result of the surgery for patient's life.

6. Uncontrolled psychotic and depressive disorder shouldn't exist.

7. Family and social environment support must be complete.

In decisions of National Institutes of Health in 1991, as a result of insufficient data, bariatric surgery wasn't recommended for morbid obese children and adolescents. However, increased prevalence and severity of childhood obesity have raised interest fort his topic, it has been proved that bariatric surgery is effective on adolescents. In this context, in the 2008 guidelines, it is suggested that the surgery should only be done in specialized centres [4]. In individuals over 60 years of age, it is emphasized that potential benefits and risks before surgery should be evaluated very well and improving the quality of life rather than prolonging the life span should be the first expectancy of the treatment [5].

Methods of Bariatric Surgery

Bariatric surgery methods, according to effect mechanism, are classified as; restrictive, absorption disruptive and combines (restrictive and absorption disruptive). Laparoscopic adjustable gastric band (LAGB), laparoscopic sleeve gastrectomy (LSG) and vertical band gastroplasty (VBG) are restrictive methods; biliopancreatic diversion (BPD), jejunoileal bypass (JIB) are absorption disruptive methods; roux-en-Y gastric bypass (RYGB), BPD and duodenal switch (DS) methods are combined methods [6,7].

Bariatric surgery methods which are frequently preferred today is RYGB, LSG, DS and BPD [8-10]. The main subject in this review article is LSG method having increasing application frequency both in our country and in the whole world and its relationship with ghrelin hormone having the main reason for the loss of weight in this method.

Laparoscopic Sleeve Gastrectomy

LSG is defined as a part of DS in 1988. Firstly, it was applied by Garner as a first step method in 1999. It is a bariatric surgical method decreasing the stomach volume and leading to restriction of nutrient intake. Primarily, LSG was used as first step of DS and BPD. If the method provides people with decreasing body weights enough and healing metabolic diseases it is declared that it can be applied as a single-stage operation [2,11,12].

LSG forms 5% of bariatric surgery. Since its surgery procedures are easier, early results are satisfactory, it is becoming a method having rising application frequency, safe and effective for surgeons and patients [12,13]. In this method stomach volume is diminished. Namely, the great curvature of this stomach is removed and it becomes a tube (Figure 1) [4,13].

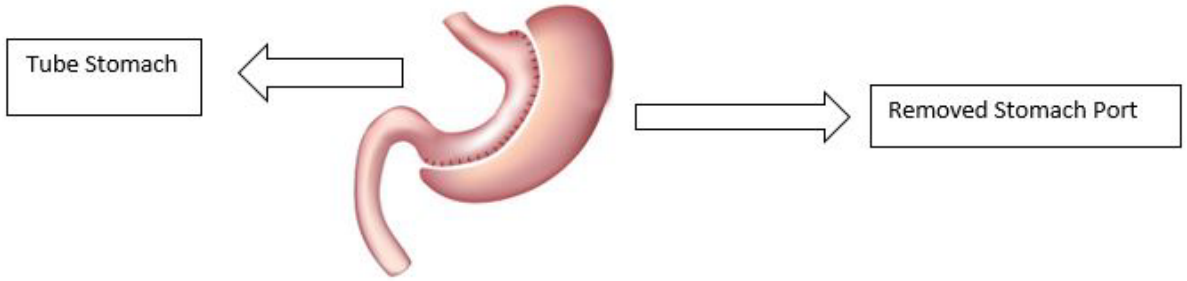

Figure 1 Sleeve gastrectomy

The advantages of LSG are;

• The operation is easier

• Anastomosis is not seen

• Malabsorption is seen rarely

• Glucose homeostasis is provided early

• There are hormonal alterations facilitating weight loss [10,14,15].

In addition, it is reported that LSG has fewer rate of mortality and morbidity than that of RYGB and DS. At the same

time LSG is used as a revision alternative for the patients who experienced unsuccessful VBG and LAGB surgery [10,14,15].

One of the most common complications of LSG is gastric leak in the gastroesophageal duct. Gastric leak may cause abdominal sepsis, gastric fistula and multi organ failure when not treated [14]. In addition, even if in LSG foregut resection is not seen, unexpected changes can be seen in distal gut hormones such as secretin and cholecystokinin [15]. Furthermore, in a study, it is reported that frequency of diseases mentioned below are much more on patients who experience LSG:

1. Hiatal hernia.

2. Gastroesophageal reflux.

3. Erosive esophagitis [16].

Incidence of hiatal hernia seen on patients experiencing LSG is 7.9 % [13].

Weight loss after bariatric surgeries is related to restrictions of nutrient intake, absorption disorders and hormonal modifications (10). In LSG restricting food intake, being a restrictive method, at the same time, as a result of stomach fundus excision, levels of some hormones secreted from stomach like gastrin change. Basically, levels of ghrelin secreted from stomach fundus and regulating food intake decrease after sleeve gastrectomy. In addition, this case is related to postoperative weight losses [11,17,18].

Ghrelin

Ghrelin is a hormone in the 28-amino acid polypeptide structure. It is firstly discovered in 1999 as a ligand for the growth hormone secretagogues matter receptor [17,18]. Apart from stomach, the hormone can be synthesized in small quantities in small intestine, hypothalamus, pituitary gland, kidney, and pancreas [19]. Ghrelin has a wide distribution in body tissues. So, this hormone plays an important role in regulating the biological activity [17].

Ghrelin has two forms in body tissues. They are acyl and desacyl ghrelin forms. Octanyl group of 8 carbons, depending on serine being amino acid the third, at terminal edge-N, is necessary for ghrelin to be active. Ghrelin acyl including octanyl group is called active ghrelin. Ghrelin not containing fatty acid is called desacyl (inactive) ghrelin [17,18,20]. The ghrelin molecular structure is given Figure 2 [21]. Half life span of carried ghrelin, dependent on HDL, in blood, is reported as 10-31 minutes. This short half-life is thought to be due to plasma esterase activity [22,23]. The plasma concentration of the hormone is 100-150 fmol/ml. On the other hand, its 80% is desacyl ghrelin, inactive form [21].

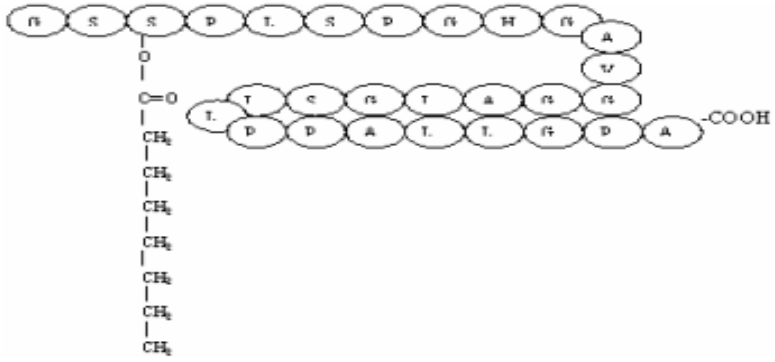

Figure 2 The ghrelin molecular structure

Ghrelin and regulation of food intake

Central and peripheral stimulation of ghrelin, an orexigenic intestinal hormone, causes an increase in food intake. Ghrelin level increases before meals and decreases depending on the increase in the amount of calories consumed in average 60-120 minutes. Therefore, ghrelin plays an important role in initiating food intake and ending meal [3,24]. Increase in hunger ghrelin levels after weight loss due to diet and exercise supports the hypothesis that ghrelin has a role in long-term regulation of body weight [3].

At the same time, ghrelin stimulates appetite and increases the amount of foods consumed. The hormone has an

appetizing effect by stimulating neuropeptide Y (NPY) and Aguoti-related protein (AgRP), from orexigenic neurons, in the arcuate nucleus of the hypothalamus; reducing α-melanocyte regulatory hormone (α-MSH) which secretes anorexigenic neuron (proopiomelanocortin/POMC) [3,18,25]. The mechanism of ghrelin on appetite is shown in Figure 3 [25]. In addition, it plays a role in regulating body weight and adiposity [3,18].

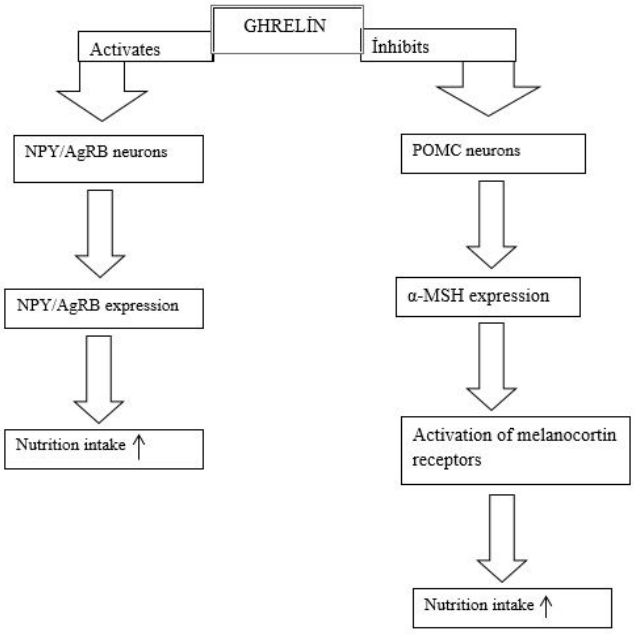

Figure 3 The mechanism of ghrelin on appetite

At the same time, the effect of ghrelin on appetite thought to be especially due to acyl ghrelin, being an active form of the hormone. Besides stimulating appetite, acyl ghrelin plays a role as gastroprotective factor by increasing gastric motility [3,18]. As the level of desacyl ghrelin, being inactive ghrelin form, it is seen that body weight and adiposity decrease, insulin sensitivity improves. As a result, it is thought that in contrast to acyl ghrelin, desacyl ghrelin may be anorexigenic hormone. However, this subject is still controversial [11].

Laparoscopic sleeve gastrectomy and ghrelin

In LSG method, since the stomach fundus, the main production centre of ghrelin, is removed it is remarked that this method may be effective on ghrelin effect mechanism [3]. Even though there are various studies regarding modifications of ghrelin levels after LSG, there is no definite conclusion about the subject [26].

In a study about the subject; ghrelin levels of 37 patients with LSG, aged between 24 and 68 years, are evaluated at the 6th and 12th months after surgery. It is seen that patients' appetite and nutrient intake decreases considerably in postoperative period. This condition is related to ghrelin levels decreased after surgery [1]. In a study evaluating LSG's long-term results, patients are evaluated in the first and 5th year, both before and after surgery. As a result, patients' plasma ghrelin levels measured at 1st and 5th year after surgery are considerably lower than the measurements made at 1st and 5th year before surgery. After surgery, at 5 years evaluation, at 1st year ghrelin levels are found high. On the other hand, it is reported that this result is not significant. In the direction of these results, it is concluded that, in the first five years after the surgery, plasma ghrelin level is low [27]. LSG method is applied to 20 patients, with type 2 diabetes mellitus, having BMI ranging from 30-35 kg/m^2. After surgery, ghrelin levels decrease considerably, at 6th month after surgery, if compared measurements before the surgery [28].

In studies [10,29-31] effects of different bariatric surgery methods on ghrelin levels are evaluated. In a study comparing LSG and RYGB methods, patients are appraised at the 3rd and 12th months both before and after surgery. The fact that ghrelin levels of patients applied RYGB approach the levels before the surgery, at the end of 12th month. In contrast, it is declared that ghrelin levels of patients applied LSG still continue to decrease at 12th month after the surgery. In another study, patients are examined at 6th and 12th weeks both before and after surgery. Hunger and postprandial acyl ghrelin levels of patients applied LSG are lower than their earlier extent. At the same time, patients

receiving RYGB [29]. Alamuddin, et al. [30] study's results are similar to the other studies. As for a study on 69 patients receiving LSG and RYGB methods; as ghrelin levels after LSG decrease, ghrelin levels after RYGB increase. However, it is emphasized that this difference doesn't affect clinical results and anthropometric measurements of patients of patients during the one-year examination period. One of the study results is that ghrelin doesn't have an obvious effect on weight loss after bariatric surgery and metabolic parameters. There are various factors being effective [31].

The effects of LSG and LAGB methods on plasma ghrelin are examined as well [32,33]. In a study associated with the subject; plasma ghrelin levels of LSG applied patients are found low at the 1st and the 6th months after the surgery if compared with the values before the surgery. On the contrary, the situation for LAGB treated patients is just the opposite. In addition, LSG applied patients have much more weight loss than patients with LAGB. This condition is related to changes in ghrelin levels (32). In another study, LSG and LAGB methods' effects on ghrelin levels for rats are examined. Fasting ghrelin levels of LAGB applied rats are higher than that of rats with LSG [33]. Kruljac, et al. [34] evaluates the effects of the three different methods on ghrelin levels. 51 patients receiving LAGB, LSg and RYGb are examined at 1st, 3rd, 6th and 12th month in respect of ghrelin levels and weight. At the end of 1st month, patients with LSG and RYGB don't have an important difference in their ghrelin levels. At the end of 1st and 3rd months, ghrelin levels of LAGb group increase significantly. There is not an important difference for LSG and RYGB group in the situation. Besides, the initial ghrelin levels of LSG applied group and the resultant weight losses at 1st and 6th months are related [34]. In a study on rats, after LSG desacyl ghrelin levels decreases, acyl ghrelin levels don't change. As different from other studies there is an interesting result. LSG affects desacyl ghrelin levels but doesn't affect acyl ghrelin levels [11]. In another study with rats, it was noted that the level of desacyl ghrelin after LSG decreased but acyl/desacyl ratio increased. As a result of reduction on desacyl ghrelin, in obese rats lipogenesis reduces. Due to relative increase an acyl ghrelin, mitochondrial oxidation and autophagy become active. Another result of the study is that, after bariatric surgery both of two isoforms of ghrelin play an important role on healing of liver fattening [35].

In Terra, et al. [18] study, in contrast to all studies cited, it is reported that, after surgery, ghrelin levels increase. In the study, effects of different surgical methods on ghrelin levels are appraised. In conclusion of all surgical methods used ghrelin levels increase in postoperative period. As a result of the study, it is claimed that this difference is due to the fact that desacyl and acyl ghrelin levels aren't evaluated separately [18].

In a review article examining the effects of LSG on plasma ghrelin levels, the results of studies about the subject are analyse. It is reported that LSG has an important effect on ghrelin levels by reducing the ghrelin level in the circulation. A conclusion of the review is that it is still hard to be sure of the end result since there is heterogeneity in data concerning studies examined [36].

CONCLUSION

Today, bariatric surgery methods are often preferred as treatment alternatives obesity. LSG is one of them. It is restrictive method. Weight loss after LSG is related to reduced nutrient intake and hormonal changes. Basically, changes in ghrelin hormone secreted from stomach fundus and playing a very important role in regulating food intake, are effective on appetite changes and weight losses after LSG. After LSG, due to stomach fundus excretion, it is expected that ghrelin hormone diminishes. On the other hand, results of the studies regarding the subject differ. Even if, as a conclusion of many studies, LSG is found very effective to reduce ghrelin levels; there are studies containing contradictory results as well. In order to understand the changes of ghrelin levels obviously after LSG and arrive a final judgement; longer termed, randomize studies more in number are required.

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